AMENDMENTS TO THE SPECIFICATION

In the specification, at page 22, lines 14-17, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

All selection criteria, as used herein, are preferably conducted in the absence of serum, to avoid the drawbacks with generating antibodies that could ~~mimick~~ mimic the pathological antibodies of patients, which bind to aminophospholipids or anionic phospholipids in conjunction with proteins.

In the specification, at page 25, lines 20-23, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

The cell impermeant group may have a positive or negative charge at physiological pH or may be polar. ~~Examplary~~ Exemplary groups include sulfate, sulfonate, phosphate, carboxyl, phenolic, quaternary ammonium ion and amine groups. A pharmaceutical composition comprising duramycin linked to biotin is a particular example within the invention.

In the specification, at page 30, lines 26-32, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Combined cancer treatment methods are those in which at least a first purified anti-aminophospholipid or anti-anionic phospholipid antibody, or antigen-binding fragment or immunoconjugate thereof, optionally one that binds to essentially the same epitope as the monoclonal antibody 3G4 (ATCC PTA 4545), or a substantially cell impermeant PE-binding peptide derivative, preferably a substantially cell impermeant duramycin derivative, is

administered to an animal or patient with cancer in ~~combiantino~~ combination with a therapeutically effective amount of at least a second, therapeutic or anti-cancer agent.

In the specification, at page 40, lines 20-26, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

FIG. 14A, FIG. 14B, FIG. 14C and FIG. 14D. Binding specificities of duramycin derivatives. The duramycin derivatives were prepared as described in Example XV and their specificities determined using ELISAs and competition ELISAs, as described in Example XVI. FIG. 14A, phospholipid binding profile of duramycin derivatives against a panel of phospholipids, showing specificity for PE; FIG. 14B, serum has no significant effect on PE binding; FIG. 14C and FIG. 14D, results from competition ELISAs ~~comfirming~~ confirming specificity of duramycin derivatives for PE.

In the specification, at page 58, lines 24-32, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

It is also possible that antibody binding to anionic phospholipids and aminophospholipids at the surface of tumor vascular endothelial cells may cause disturbances in the ~~cytoskeletalal~~ cytoskeletal organization of the cell. As the cytoskeleton plays a role in the organization of surface membranes, and as antibody binding may disturb (or further disturb) the membrane, binding of antibodies to anionic phospholipids and aminophospholipids may transmit changes to cytoskeletal proteins that interact with the bilayer. It is already known that the spatial organization of cytoskeletal proteins controls membrane stability and cell shape, and it is

possible that perturbation of some cytoskeletal equilibrium may have far-reaching consequences on cell integrity.

In the specification, from page 63, line 33 to page 64, line 4, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

The present invention provides "second generation" antibodies that bind to aminophospholipids and anionic phospholipids, which antibodies have improved properties and/or do not ~~suffere~~ suffer from the drawback associated with the antibodies in the prior art. A panel of such antibodies is disclosed herein, of which the monoclonal antibodies 9D2 and 3G4 are currently preferred, with the 3G4 (ATCC 4545) antibody being particularly preferred. The invention also provides particular immunization and screening techniques, which permit "like" or "competing" antibodies with advantageous properties and/or less drawbacks to be produced.

In the specification, at page 117, lines 18-23, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Depending on the specific agents to be conjugated, it may be necessary or desirable to provide a peptide spacer operatively attaching the antibody or PE-binding peptide and the second or therapeutic agent. ~~Cetain~~ Certain peptide spacers are capable of folding into a disulfide-bonded loop structure. Proteolytic cleavage within the loop would then yield a heterodimeric polypeptide wherein the antibody and the therapeutic agent are linked by only a single disulfide bond. An example of such a toxin is a Ricin A-chain toxin.

In the specification, from page 158, line 34 to page 159, line 4, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Drugs that induce apoptosis are preferred for use in the ~~combinaition~~ combination therapies. Docetaxel, for example, induces apoptosis and therefore PS exposure by binding to microtubules and disrupting cell mitosis (Hotchkiss *et al.*, 2002). Treatment of endothelial cells, which line tumor blood vessels, and tumor cells with docetaxel at subclinical concentrations is herein shown to induce PS expression at the cell surface, as demonstrated by strong binding of the 3G4 antibody *in vitro*.

In the specification, at page 176, lines 18-23, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Moreover, the antibody-coated stealthed liposomes of the invention may also be loaded with one or more anti-viral drugs for use in treating viral infections and diseases. As with the anti-cancer agents, any one or more of the second, anti-viral drugs known in the art and/or described herein for conjugation to antibodies, or for combination therapies, may be used in the antibody-coated stealthed liposomes of the invention. ~~Cidofavir~~ Cidofovir and AZT are currently preferred examples.

In the specification, at page 182, lines 13-21, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Within this category of PE-binding peptide derivatives, certain constructs will emphasize the recruitment of host defenses, thus ~~enhacing~~ enhancing their therapeutic activity. For example, where a PE-binding peptide, preferably duramycin, is attached to an immunoglobulin,

example, where a PE-binding peptide, preferably duramycin, is attached to an immunoglobulin, the immunoglobulin can function both as an inert carrier and as an immune effector. This applies to immunoglobulins of so-called "irrelevant specificity" and to immunoglobulin derivatives without antigen binding capacity, such as Fc regions. By virtue of the attached immunoglobulin or immunoglobulin derivative, such constructs will be able to redirect host defenses against PE-expressing cells, *e.g.* by attracting and/or activating immune effector cells.

In the specification, at page 183, lines 7-12, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Any of the conjugation techniques ~~decribed~~ described above may be used to prepare duramycin derivatives in accordance with the invention, including cross-linkers, peptide spacers, biotin:avidin constructs and recombinant expression. An advantageous site of attachment within the duramycin molecule, for example, is to the lysine residue at amino acid position 2 in the duramycin sequence (SEQ ID NO:9; FIG. 13P; Hayashi *et al.*, 1990). However, linkage at this site is not a requirement of the invention.

In the specification, at page 196, lines 10-14, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

As the PE-binding peptide derivatives localize to macrophages in the lung after systemic administration will naturally be effective. Administration to the lung by more direct means, including via aerosol, is also envisioned. The present invention therefore solves important deficiencies in the viral treatment field ~~bu~~ by providing widely applicable and practical anti-viral remedies.

In the specification, at page 279, lines 10-16, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

The 3G4 antibody is also shown to be very effective in inhibiting CMV, both *in vitro* (Example XII) and in enhancing the survival of mice infected with mCMV *in vivo* (Example XXI). In addition, the 3G4 antibody is further shown to inhibit Pichinde virus infection, the infectious agent of Lassa fever (Example XXIV). The cell surface PS exposure herein shown to follow viral infection, and the ability of the 3G4 antibody to bind to cells infected with Vaccinia virus (Example XXIII), shows that the 3G4 antibody has enormous potential as a broad ~~spectum~~ spectrum anti-viral agent.

In the specification, at page 289, lines 15-23, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

Using the same MethA mouse tumor model as above, when the tumor size reach 500 mm^3, 100 μg $(D\text{-}SIAB)_n$HIgG in 100 μl PBS was injected through the tail vein. The same amount of human IgG was injected as a control. After 4 hours, mice was euthanized and perfused with normal saline for 5 minutes and 1% paraformadehyde for 10 minutes. The tumor and other major organs were dissected and frozen in liquid nitrogen. After embedding in OCT, tissue was cryosected in 10 μm section and placed on silanized slides. After fixing in cold acetone for 10 minutes, slides were stained with peroxidase labeled goat anti human IgG to ~~dectect~~ detect the biodistribution of duramycin-HuIgG. Meca32 and peroxidase labeled goat anti-rat IgG were used to detect blood vasculature of tissue.

In the specification, at page 290, lines 11-20, please delete the existing paragraph and replace with the following paragraph after implementing the following changes:

The human breast cancer cell line MDA-MB-435 was grown, harvested at log phase, and resuspended in DPBS. Approximately 10^7 cells were injected into the mammary fat pad of 6-8 week old female athymic nude mice. 100 μg duramycin-biotin in 100 μl PBS was injected through the tail vein. After 4 hours, mice was euthanized and perfused with normal saline for 5 minutes and 1% paraformadehyde for 10 minutes. Major organs, including heart, lung, liver, kidney, brain, intestine, testes and spleen were dissected and frozen in liquid nitrogen. After embedding in OCT, tissue was cryosected in 10 μm sections and placed on silanized slides. After fixing in cold acetone for 10 minutes, slides were stained with Cy3 labeled ~~strepavidin~~ streptavidin to ~~dectect~~ detect the biodistribution of the duramycin-biotin construct. Meca32 and FITC labeled goat anti rat IgG were used to detect blood vasculature of tissue.